

**REMARKS**

**I.** The application is being amended to insert information regarding U.S. government support for research that lead to the invention now being claimed.

No new matter is being added. Entry of the amendment is respectfully requested.

**II.** This paper is also responsive to the Advisory Action mailed December 31, 2007. Therein, the Examiner indicates that the Amendment filed November 30, 2007, does not place the application in condition for allowance. In particular, claim 1 remains rejected under 35 U.S.C. §103 for the reasons of record.

In response, Applicants respectfully note that claim 1 has been canceled. It appears that the Examiner intended to refer to claim 5.

Applicants further respectfully note that because claim 6 was previously indicated as being allowable, and because claim 5 (as now pending) is of the same scope as claim 6, claim 5 should also be allowable. Indeed, in the Advisory Action the Examiner refers to “the reasons previously set forth in the paper mailed 7/12/07, Section 7, pages 3-4” as the reasons of record for maintaining the rejection. This citation is to the rejection of claims 5, 7 and 38. The subject matter of claim 6 (now recited in claim 5) is not included in this rejection.

In further support of the allowability of claim 5, Applicants have the following comments. Section 7, pages 3-4 of the office action dated July 12, 2007 (cited in the Advisory Action), cites back through to an office action dated June 17, 2005, wherein claims to antibodies binding the polypeptide of the present invention were rejected over Purnelle et al. or Kirby et al., and further in view of Harlow et al. (complete citations provided in the office action). Thus, Applicants understand the “reasons of record” mentioned in the Advisory Action to be the rejection under 35 U.S.C. §103, over Purnelle et al., Kirby et al. and Harlow et al., first set forth in the office action dated June 17, 2005.

The art cited by the Examiner (Purnelle et al. and Kirby et al.) pertains to two polypeptides, with very low degrees of overall homology to the polypeptide of SEQ ID NO:1 of the pending application (30.5% and 32.1%, respectively). While certain regions of the

polypeptides of Purnelle et al. and Kirby et al. appear to have homology to regions of the polypeptide of SEQ ID NO:1, such regions are limited to only a small number of contiguous amino acids (seven or fewer).

Applicants again respectfully assert that none of the art of record teaches or suggests the monoclonal antibody of claim 5. Neither of the two publications teaches antibodies against the polypeptide of SEQ ID NO:1, let alone monoclonal antibodies against the polypeptide of SEQ ID NO:1. Furthermore, neither of the two publications provides any information regarding immunodominant regions of the polypeptides they disclose. While there may be regions of homology between the polypeptides of the cited art and the polypeptide of SEQ ID NO:1, such regions are quite small (seven or fewer amino acids) and there is nothing in any of the art cited by the Examiner to suggest that these region are immunodominant, that is, there is nothing to suggest that these regions are of sufficient antigenicity such that antibodies would be raised that would recognize and bind these regions.

Applicants note that the three dimensional structure of a polypeptide is of fundamental importance in the formation of particular antigenic determinants of a protein. Herbert et al. (the Dictionary of Immunology, Academic Press, 4th Edition, London, 1985, pages 58-59, already of record) teaches that epitopes are regions of polypeptides to which antibodies specifically bind, and that such binding is based on an exact three-dimensional fit. Further, epitopes are formed by residues on different portions of the polypeptide, brought together by the native folding of the protein. Harlow further notes that the three dimensional structure of the protein may be essential for antibody binding.

A publication by Flower (*Trends Immunol.* 2003, 24:667-674; a copy of which is enclosed) further supports this position. As noted therein, it is quite difficult to accurately predict whether a particular region of a protein will be immunogenic (page 667, right column, first full paragraph). Indeed, as discussed throughout the publication, there is no consistently accurate means for accurately predicting whether a particular region of a polypeptide will be immunogenic.

Nothing in either Purnelle et al. or Kirby et al. provides information regarding the folding of the polypeptides taught therein, or any antigenic determinants of those polypeptides. Thus, neither Purnelle et al. nor Kirby et al. teaches which residues might be critical for forming antigenic determinants of the proteins. In the absence of such guidance, the skilled artisan would not expect that those small regions of homology between the polypeptides of Purnelle et al. and Kirby et al., and the polypeptide of SEQ ID NO:1, would serve as immunodominant regions of the polypeptides. Indeed, in view of the teachings of Harlow et al. with regard to the formation of epitopes based on residues from different parts of the protein being brought into proximity by protein folding, and the low degree of overall homology between the polypeptides of the cited art and the polypeptide of SEQ ID NO:1, the skilled artisan would not expect that antibodies that specifically bind the polypeptides of Purnelle et al. and Kirby et al. would also bind the polypeptide of SEQ ID NO:1.

Applicants also note that the native glycosylation of a polypeptide can contribute to antibody specificity. Neither Purnelle et al. nor Kirby et al. provides any information regarding the glycosylation of the polypeptides taught therein. Such an absence of information further contributes to the lack of obviousness of the pending claims.

In view of the above amendments and remarks, it is clear that the monoclonal antibodies of the pending claims are novel and non-obvious. Therefore, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

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Respectfully submitted,

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